

## PATENT COOPERATION TREATY

PCT

## NOTIFICATION OF ELECTION

(PCT Rule 61.2)

From the INTERNATIONAL BUREAU

To:

Assistant Commissioner for Patents  
 United States Patent and Trademark  
 Office  
 Box PCT  
 Washington, D.C.20231  
 ÉTATS-UNIS D'AMÉRIQUE

in its capacity as elected Office

|  |  |
|--|--|
| Date of mailing (day/month/year)<br>22 November 1999 (22.11.99)        |  |
| International application No.<br>PCT/EP99/01966                        | Applicant's or agent's file reference<br>PG3376/PCT        |
| International filing date (day/month/year)<br>24 March 1999 (24.03.99) | Priority date (day/month/year)<br>26 March 1998 (26.03.98) |
| <b>Applicant</b><br><br>MARRIOTT, Christopher et al                    |  |

1. The designated Office is hereby notified of its election made:

in the demand filed with the International Preliminary Examining Authority on:

07 October 1999 (07.10.99)

in a notice effecting later election filed with the International Bureau on:

\_\_\_\_\_

2. The election  was

was not

made before the expiration of 19 months from the priority date or, where Rule 32 applies, within the time limit under Rule 32.2(b).

|   |   |
|---|---|
| The International Bureau of WIPO<br>34, chemin des Colombettes<br>1211 Geneva 20, Switzerland<br><br>Facsimile No.: (41-22) 740.14.35 | Authorized officer<br><br>F. Baechler<br><br>Telephone No.: (41-22) 338.83.38 |
|---|---|

## PATENT COOPERATION TREATY

PCT

NOTIFICATION OF THE RECORDING  
OF A CHANGE(PCT Rule 92bis.1 and  
Administrative Instructions, Section 422)

|  |
|--|
| Date of mailing (day/month/year)<br>13 September 2000 (13.09.00) |
|--|

From the INTERNATIONAL BUREAU

To:

CRAWLEY, Karen  
 Glaxo Wellcome plc  
 Glaxo Wellcome House  
 Berkeley Avenue  
 Greenford  
 Middlesex UB6 0NN  
 ROYAUME-UNI

|   |
|---|
| Applicant's or agent's file reference<br>PG3376/PCT |
|---|

## IMPORTANT NOTIFICATION

|   |
|---|
| International application No.<br>PCT/EP99/01966 |
|---|

|  |
|--|
| International filing date (day/month/year)<br>24 March 1999 (24.03.99) |
|--|

## 1. The following indications appeared on record concerning:

|   |  |                                    |  |
|---|--|------------------------------------|--|
| <input checked="" type="checkbox"/> the applicant | <input checked="" type="checkbox"/> the inventor | <input type="checkbox"/> the agent | <input type="checkbox"/> the common representative |
|---|--|------------------------------------|--|

## Name and Address

MARTIN, Gary, Peter  
 King's College London  
 Manresa Road  
 London SW3 6LX  
 United Kingdom

## State of Nationality

GB

## State of Residence

GB

Telephone No.

Facsimile No.

Teleprinter No.

## 2. The International Bureau hereby notifies the applicant that the following change has been recorded concerning:

|                                     |                                   |   |  |  |
|-------------------------------------|-----------------------------------|---|--|--|
| <input type="checkbox"/> the person | <input type="checkbox"/> the name | <input checked="" type="checkbox"/> the address | <input type="checkbox"/> the nationality | <input type="checkbox"/> the residence |
|-------------------------------------|-----------------------------------|---|--|--|

## Name and Address

MARTIN, Gary, Peter  
 King's College London  
 Franklin-Wilkins Building  
 London SE18WA  
 United Kingdom

## State of Nationality

GB

## State of Residence

GB

Telephone No.

Facsimile No.

Teleprinter No.

## 3. Further observations, if necessary:

## 4. A copy of this notification has been sent to:

|   |   |
|---|---|
| <input checked="" type="checkbox"/> the receiving Office                              | <input type="checkbox"/> the designated Offices concerned         |
| <input type="checkbox"/> the International Searching Authority                        | <input checked="" type="checkbox"/> the elected Offices concerned |
| <input checked="" type="checkbox"/> the International Preliminary Examining Authority | <input type="checkbox"/> other:                                   |

|   |   |
|---|---|
| The International Bureau of WIPO<br>34, chemin des Colombettes<br>1211 Geneva 20, Switzerland<br><br>Facsimile No.: (41-22) 740.14.35 | Authorized officer<br><br>Athina Nickitas-Etienne<br><br>Telephone No.: (41-22) 338.83.38 |
|---|---|

## ATTENT COOPERATION TRE, Y

From the INTERNATIONAL BUREAU

PCT

NOTIFICATION OF THE RECORDING  
OF A CHANGE(PCT Rule 92bis.1 and  
Administrative Instructions, Section 422)

|  |
|--|
| Date of mailing (day/month/year)<br>13 September 2000 (13.09.00) |
| Applicant's or agent's file reference<br>PG3376/PCT              |
| International application No.<br>PCT/EP99/01966                  |

To:

CRAWLEY, Karen  
 Glaxo Wellcome plc  
 Glaxo Wellcome House  
 Berkeley Avenue  
 Greenford  
 Middlesex UB6 0NN  
 ROYAUME-UNI

## IMPORTANT NOTIFICATION

International filing date (day/month/year)  
24 March 1999 (24.03.99)

## 1. The following indications appeared on record concerning:

the applicant     the inventor     the agent     the common representative

|  |                            |                          |
|--|----------------------------|--------------------------|
| Name and Address<br><br>MARRIOTT, Christopher<br>King's College London<br>Manresa Road<br>London SW3 6LX<br>United Kingdom | State of Nationality<br>GB | State of Residence<br>GB |
|  | Telephone No.              |                          |
|  | Facsimile No.              |                          |
|  | Teleprinter No.            |                          |

## 2. The International Bureau hereby notifies the applicant that the following change has been recorded concerning:

the person     the name     the address     the nationality     the residence

|  |                            |                          |
|--|----------------------------|--------------------------|
| Name and Address<br><br>MARRIOTT, Christopher<br>King's College London<br>Franklin-Wilkins Building<br>London SE18WA<br>United Kingdom | State of Nationality<br>GB | State of Residence<br>GB |
|  | Telephone No.              |                          |
|  | Facsimile No.              |                          |
|  | Teleprinter No.            |                          |

## 3. Further observations, if necessary:

## 4. A copy of this notification has been sent to:

|   |   |
|---|---|
| <input checked="" type="checkbox"/> the receiving Office                              | <input type="checkbox"/> the designated Offices concerned         |
| <input type="checkbox"/> the International Searching Authority                        | <input checked="" type="checkbox"/> the elected Offices concerned |
| <input checked="" type="checkbox"/> the International Preliminary Examining Authority | <input type="checkbox"/> other:                                   |

|   |   |
|---|---|
| The International Bureau of WIPO<br>34, chemin des Colombettes<br>1211 Geneva 20, Switzerland<br><br>Facsimile No.: (41-22) 740.14.35 | Authorized officer<br><br>Athina Nickitas-Etienne<br><br>Telephone No.: (41-22) 338.83.38 |
|---|---|

## ATENT COOPERATION TRE, Y

PCT

NOTIFICATION OF THE RECORDING  
OF A CHANGE(PCT Rule 92bis.1 and  
Administrative Instructions, Section 422)

|  |
|--|
| Date of mailing (day/month/year)<br>13 September 2000 (13.09.00) |
|--|

From the INTERNATIONAL BUREAU

To:

CRAWLEY, Karen  
 Glaxo Wellcome plc  
 Glaxo Wellcome House  
 Berkeley Avenue  
 Greenford  
 Middlesex UB6 0NN  
 ROYAUME-UNI

|   |  |  |  |
|---|--|--|--|
| Applicant's or agent's file reference<br>PG3376/PCT | <b>IMPORTANT NOTIFICATION</b>  |  |  |
| International application No.<br>PCT/EP99/01966     | International filing date (day/month/year)<br>24 March 1999 (24.03.99) |  |  |

## 1. The following indications appeared on record concerning:

the applicant     the inventor     the agent     the common representative

|   |                            |                          |
|---|----------------------------|--------------------------|
| Name and Address<br><br>ZENG, Xian, Ming<br>King's College London<br>Manresa Road<br>London SW3 6LX<br>United Kingdom | State of Nationality<br>CN | State of Residence<br>GB |
|   | Telephone No.              |                          |
|   | Facsimile No.              |                          |
|   | Teleprinter No.            |                          |

## 2. The International Bureau hereby notifies the applicant that the following change has been recorded concerning:

the person     the name     the address     the nationality     the residence

|   |                            |                          |
|---|----------------------------|--------------------------|
| Name and Address<br><br>ZENG, Xian, Ming<br>King's College London<br>Franklin-Wilkins Building<br>London SE18WA<br>United Kingdom | State of Nationality<br>CN | State of Residence<br>GB |
|   | Telephone No.              |                          |
|   | Facsimile No.              |                          |
|   | Teleprinter No.            |                          |

## 3. Further observations, if necessary:

## 4. A copy of this notification has been sent to:

|   |   |
|---|---|
| <input checked="" type="checkbox"/> the receiving Office                              | <input type="checkbox"/> the designated Offices concerned         |
| <input type="checkbox"/> the International Searching Authority                        | <input checked="" type="checkbox"/> the elected Offices concerned |
| <input checked="" type="checkbox"/> the International Preliminary Examining Authority | <input type="checkbox"/> other:                                   |

|   |   |
|---|---|
| The International Bureau of WIPO<br>34, chemin des Colombettes<br>1211 Geneva 20, Switzerland<br><br>Facsimile No.: (41-22) 740.14.35 | Authorized officer<br><br>Athina Nickitas-Etienne<br><br>Telephone No.: (41-22) 338.83.38 |
|---|---|

## PCT COOPERATION TREATY

09/646/11

PCT

NOTIFICATION OF THE RECORDING  
OF A CHANGE(PCT Rule 92bis.1 and  
Administrative Instructions, Section 422)

|   |
|---|
| Date of mailing (day/month/year)<br>03 November 2000 (03.11.00) |
| Applicant's or agent's file reference<br>PG3376/PCT             |
| International application No.<br>PCT/EP99/01966                 |

From the INTERNATIONAL BUREAU

To:

CRAWLEY, Karen  
 Glaxo Wellcome plc  
 Glaxo Wellcome House  
 Berkeley Avenue  
 Greenford  
 Middlesex UB6 0NN  
 ROYAUME-UNI

## IMPORTANT NOTIFICATION

|  |
|--|
| International filing date (day/month/year)<br>24 March 1999 (24.03.99) |
|--|

1. The following indications appeared on record concerning:

the applicant     the inventor     the agent     the common representative

|   |                            |                          |
|---|----------------------------|--------------------------|
| Name and Address<br><br>ZENG, Xian, Ming<br>King's College London<br>Manresa Road<br>London SW3 6LX<br>United Kingdom | State of Nationality<br>CN | State of Residence<br>GB |
|   | Telephone No.              |                          |
|   | Facsimile No.              |                          |
|   | Teleprinter No.            |                          |

2. The International Bureau hereby notifies the applicant that the following change has been recorded concerning:

the person     the name     the address     the nationality     the residence

|  |                            |                          |
|--|----------------------------|--------------------------|
| Name and Address<br><br>ZENG, Xian, Ming<br>14 Newburgh Road<br>Rectory Gardens<br>Grays, Essex RM17 6UG<br>United Kingdom | State of Nationality<br>CN | State of Residence<br>GB |
|  | Telephone No.              |                          |
|  | Facsimile No.              |                          |
|  | Teleprinter No.            |                          |

3. Further observations, if necessary:

4. A copy of this notification has been sent to:

|   |   |
|---|---|
| <input checked="" type="checkbox"/> the receiving Office                              | <input type="checkbox"/> the designated Offices concerned         |
| <input type="checkbox"/> the International Searching Authority                        | <input checked="" type="checkbox"/> the elected Offices concerned |
| <input checked="" type="checkbox"/> the International Preliminary Examining Authority | <input type="checkbox"/> other:                                   |

|   |   |
|---|---|
| The International Bureau of WIPO<br>34, chemin des Colombettes<br>1211 Geneva 20, Switzerland<br><br>Facsimile No.: (41-22) 740.14.35 | Authorized officer<br><br>Athina Nickitas-Etienne<br><br>Telephone No.: (41-22) 338.83.38 |
|---|---|

**PATENT COOPERATION TREATY**  
21 JUL 2000

**PCT**

IPO

PCT

**INTERNATIONAL PRELIMINARY EXAMINATION REPORT**

**(PCT Article 36 and Rule 70)**

|   |  |   |
|---|--|---|
| Applicant's or agent's file reference<br><br>PG3376/pct   | <b>FOR FURTHER ACTION</b>                                    | See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416) |
| International application No.<br><br>PCT/EP99/01966   | International filing date (day/month/year)<br><br>24/03/1999 | Priority date (day/month/year)<br><br>26/03/1998  |
| International Patent Classification (IPC) or national classification and IPC<br><br>A61K9/00  |  |   |
| <p><b>Applicant</b><br/><br/>GLAXO GROUP LIMITED</p>  |  |   |
| <p>1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.</p> <p>2. This REPORT consists of a total of 5 sheets, including this cover sheet.</p> <p><input type="checkbox"/> This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).</p> <p>These annexes consist of a total of sheets.</p>   |  |   |
| <p>3. This report contains indications relating to the following items:</p> <ul style="list-style-type: none"> <li>I    <input checked="" type="checkbox"/> Basis of the report</li> <li>II   <input type="checkbox"/> Priority</li> <li>III   <input type="checkbox"/> Non-establishment of opinion with regard to novelty, inventive step and industrial applicability</li> <li>IV   <input type="checkbox"/> Lack of unity of invention</li> <li>V   <input checked="" type="checkbox"/> Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement</li> <li>VI   <input type="checkbox"/> Certain documents cited</li> <li>VII   <input type="checkbox"/> Certain defects in the international application</li> <li>VIII   <input type="checkbox"/> Certain observations on the international application</li> </ul> |  |   |

|   |   |
|---|---|
| Date of submission of the demand<br><br>07/10/1999  | Date of completion of this report<br><br>19.07.2000                         |
| Name and mailing address of the international preliminary examining authority:<br><br>European Patent Office<br>D-80298 Munich<br>Tel. +49 89 2399 - 0 Tx: 523656 epmu d<br>Fax: +49 89 2399 - 4465 | Authorized officer<br><br>Stoltner, A<br><br>Telephone No. +49 89 2399 8408 |



**INTERNATIONAL PRELIMINARY  
EXAMINATION REPORT**

International application No. PCT/EP99/01966

**I. Basis of the report**

1. This report has been drawn on the basis of (*substitute sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to the report since they do not contain amendments.*):

**Description, pages:**

1-28                   as originally filed

**Claims, No.:**

1-18                   as originally filed

**Drawings, sheets:**

1/3-3/3               as originally filed

2. The amendments have resulted in the cancellation of:

the description,      pages:  
 the claims,           Nos.:  
 the drawings,         sheets:

3.  This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)):

4. Additional observations, if necessary:

**INTERNATIONAL PRELIMINARY  
EXAMINATION REPORT**

International application No. PCT/EP99/01966

**V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

**1. Statement**

|                               |      |             |
|-------------------------------|------|-------------|
| Novelty (N)                   | Yes: | Claims 1-18 |
|                               | No:  | Claims      |
| Inventive step (IS)           | Yes: | Claims 1-18 |
|                               | No:  | Claims      |
| Industrial applicability (IA) | Yes: | Claims 1-18 |
|                               | No:  | Claims      |

**2. Citations and explanations**

**see separate sheet**

**ad section V:**

- 1). The present application concerns a process for manufacturing crystals with particular characteristics such as controlled surface-smoothness, size, shape and degree of crystallinity. Said crystals with a particularly well defined morphology results find use in the manufacture of pharmaceutical inhaled formulations exhibiting advantageous properties. Said crystals are manufactured by a crystallisation process as depicted under steps (a)-(e) in claim 1.
- 2). With respect to the present subject-matter the following documents have been researched and considered:
  - D1, WO-A-9 505 805, relates to a process for providing a stable crystalline form of a fine-grained substance, comprising lactose and active ingredients such as salbutamol or ipratropium (cf. abstract and page 6, lines 16-31 and page 7, lines 4-36). On page 4, lines 23-36 and page 5, lines 1-14, D1 describes the process of how to obtain such stable crystals. D1, however, does nowhere refer to a crystallisation method whereby the viscosity of the crystallisation medium is adjusted as presently depicted.
  - D2, WO-A-9 623 485, concerns the method of producing a powder for use in dry powder inhalers (cf. page 24, last line bridging with page 25, lines 1-14). Said powder includes active particles (cf. page 18, lines 15-18) and carrier particles (lactose) for carrying the active particles and further includes also additive material (a glidant) which is attached to the surfaces of the carrier particles in order to promote the release of the hereto attached active particles. D2, however, is silent on a crystallisation process as presently claimed and compositions containing such crystals.
  - D3, WO-A-9 638 153, provides amorphous stable solid dispersions of misoprostol, using excipients like carbopol in an amorphous state and lactose in crystalline form (cf. page 3, "Summary of the invention", lines 1-26, page 4, lines 12-34, and page 5, first line).

D4, International Journal of Pharmaceutics, 116(1), march 1995, pp. 113-118, G. Buckton et al., studies the use of isothermal microcalorimetry in the change of crystallinity of spray-dried salbutamol sulfate (cf. abstract). D4 shows that salbutamol sulfate recrystallizes in water vapour by a cooperative process and compares salbutamol recrystallization with data for the recrystallization of spray-dried lactose. There is however, no reference to a crystallization process as presently depicted.

3). A crystallization process as defined in steps (a)-(e) of claim 1 is nowhere disclosed nor suggested in the cited documents. As consequence the skilled man in art would by no means be led to the crystals resulting from said process and to the inhaler formulations manufactured by way of said process. In the light of the above cited documents the subject-matter of the present set of claims has to be recognised both novel and inventive pursuant to Arts. 33(2) and 33(3) PCT.

## PATENT COOPERATION TREATY

## PCT

## INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

|  |   |  |
|--|---|--|
| Applicant's or agent's file reference<br><b>PG3376/pct</b> | <b>FOR FURTHER ACTION</b> see Notification of Transmittal of International Search Report (Form PCT/ISA/220) as well as, where applicable, item 5 below. |  |
| International application No.<br><b>PCT/EP 99/ 01966</b>   | International filing date (day/month/year)<br><b>24/03/1999</b>   | (Earliest) Priority Date (day/month/year)<br><b>26/03/1998</b> |
| Applicant<br><b>GLAXO GROUP LIMITED</b>                    |   |  |

This International Search Report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This International Search Report consists of a total of 3 sheets.

It is also accompanied by a copy of each prior art document cited in this report.

1. Basis of the report

- a. With regard to the language, the international search was carried out on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.
  - the international search was carried out on the basis of a translation of the international application furnished to this Authority (Rule 23.1(b)).
- b. With regard to any nucleotide and/or amino acid sequence disclosed in the international application, the international search was carried out on the basis of the sequence listing :
  - contained in the international application in written form.
  - filed together with the international application in computer readable form.
  - furnished subsequently to this Authority in written form.
  - furnished subsequently to this Authority in computer readable form.
  - the statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
  - the statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished

2.  Certain claims were found unsearchable (See Box I).

3.  Unity of invention is lacking (see Box II).

4. With regard to the title,

- the text is approved as submitted by the applicant.
- the text has been established by this Authority to read as follows:

**IMPROVED CRYSTAL STRUCTURE**

5. With regard to the abstract,

- the text is approved as submitted by the applicant.
- the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box III. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

6. The figure of the drawings to be published with the abstract is Figure No.

- as suggested by the applicant.
- because the applicant failed to suggest a figure.
- because this figure better characterizes the invention.

None of the figures.



## INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

|   |    |  |
|---|----|--|
| (51) International Patent Classification <sup>6</sup> :<br><br>A61K 9/00, 9/12, 31/135  | A1 | (11) International Publication Number: <b>WO 99/48475</b><br><br>(43) International Publication Date: 30 September 1999 (30.09.99)   |
| (21) International Application Number: PCT/EP99/01966   |    | (81) Designated States: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, ARIPO patent (GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG). |
| (22) International Filing Date: 24 March 1999 (24.03.99)  |    |  |
| (30) Priority Data:<br>9806477.7 26 March 1998 (26.03.98) GB  |    |  |
| (71) Applicant ( <i>for all designated States except US</i> ): GLAXO GROUP LIMITED [GB/GB]; Glaxo Wellcome House, Berkeley Avenue, Greenford, Middlesex UB6 0NN (GB).   |    |  |
| (72) Inventors; and   |    |  |
| (75) Inventors/Applicants ( <i>for US only</i> ): MARRIOTT, Christopher [GB/GB]; King's College London, Manresa Road, London SW3 6LX (GB). MARTIN, Gary, Peter [GB/GB]; King's College London, Manresa Road, London SW3 6LX (GB). ZENG, Xian, Ming [CN/GB]; King's College London, Manresa Road, London SW3 6LX (GB). |    | <b>Published</b><br><i>With international search report.<br/>Before the expiration of the time limit for amending the claims and to be republished in the event of the receipt of amendments.</i>  |
| (74) Agent: CRAWLEY, Karen; Glaxo Wellcome plc, Glaxo Wellcome House, Berkeley Avenue, Greenford, Middlesex UB6 0NN (GB).   |    |  |

(54) Title: IMPROVED CRYSTAL STRUCTURE

## (57) Abstract

A process for the production of crystals with controlled surface smoothness, size, shape and degree of crystallinity, compositions comprising such crystals, and the use of certain crystals, especially lactose, lactose monohydrate, fluticasone propionate, salmeterol xinafoate, salbutamol sulphate or ipratropium bromide in pharmaceutical compositions.

***FOR THE PURPOSES OF INFORMATION ONLY***

Codes used to identify States party to the PCT on the front pages of pamphlets publishing international applications under the PCT.

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| AM | Amenia                   | FI | Finland                               | LT | Lithuania                                 | SK | Slovakia                 |
| AT | Austria                  | FR | France                                | LU | Luxembourg                                | SN | Senegal                  |
| AU | Australia                | GA | Gabon                                 | LV | Latvia                                    | SZ | Swaziland                |
| AZ | Azerbaijan               | GB | United Kingdom                        | MC | Monaco                                    | TD | Chad                     |
| BA | Bosnia and Herzegovina   | GE | Georgia                               | MD | Republic of Moldova                       | TG | Togo                     |
| BB | Barbados                 | GH | Ghana                                 | MG | Madagascar                                | TJ | Tajikistan               |
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| BG | Bulgaria                 | HU | Hungary                               | MN | Mongolia                                  | TT | Trinidad and Tobago      |
| BJ | Benin                    | IE | Ireland                               | MR | Mauritania                                | UA | Ukraine                  |
| BR | Brazil                   | IL | Israel                                | MW | Malawi                                    | UG | Uganda                   |
| BY | Belarus                  | IS | Iceland                               | MX | Mexico                                    | US | United States of America |
| CA | Canada                   | IT | Italy                                 | NE | Niger                                     | UZ | Uzbekistan               |
| CF | Central African Republic | JP | Japan                                 | NL | Netherlands                               | VN | Viet Nam                 |
| CG | Congo                    | KE | Kenya                                 | NO | Norway                                    | YU | Yugoslavia               |
| CH | Switzerland              | KG | Kyrgyzstan                            | NZ | New Zealand                               | ZW | Zimbabwe                 |
| CI | Côte d'Ivoire            | KP | Democratic People's Republic of Korea | PL | Poland                                    |    |                          |
| CM | Cameroon                 | KR | Republic of Korea                     | PT | Portugal                                  |    |                          |
| CN | China                    | KZ | Kazakhstan                            | RO | Romania                                   |    |                          |
| CU | Cuba                     | LC | Saint Lucia                           | RU | Russian Federation                        |    |                          |
| CZ | Czech Republic           | LI | Liechtenstein                         | SD | Sudan                                     |    |                          |
| DE | Germany                  | LK | Sri Lanka                             | SE | Sweden                                    |    |                          |
| DK | Denmark                  | LR | Liberia                               | SG | Singapore                                 |    |                          |
| EE | Estonia                  |    |                                       |    |   |    |                          |

# INTERNATIONAL SEARCH REPORT

International Application No

PCT/EP 99/01966

**A. CLASSIFICATION OF SUBJECT MATTER**

IPC 6 A61K9/00 A61K9/12 A61K31/135

According to International Patent Classification (IPC) or to both national classification and IPC

**B. FIELDS SEARCHED**

Minimum documentation searched (classification system followed by classification symbols)

IPC 6 A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

**C. DOCUMENTS CONSIDERED TO BE RELEVANT**

| Category ° | Citation of document, with indication, where appropriate, of the relevant passages   | Relevant to claim No. |
|------------|--|-----------------------|
| Y          | <p>WO 95 05805 A (ASTRA AB ;BRIGGNER LARS ERIK (SE); TROFAST EVA ANN CHRISTIN (SE))<br/>           2 March 1995 (1995-03-02)<br/>           *cf. abstract, page 1,1st para., page 4,<br/>           lines 23-38 bridging with page 5, lines<br/>           1-14, page 6, lines 21-31 and page 7,<br/>           lines 4-15*</p> <p>---</p> <p>WO 96 23485 A (CO ORDINATED DRUG DEV ;STANIFORTH JOHN NICHOLAS (GB))<br/>           8 August 1996 (1996-08-08)<br/>           *cf. abstract, page 4, lines 9-26, page<br/>           24, last line bridging with page 25, lines<br/>           1-14, claims*</p> <p>---</p> <p>---</p> | 1-18                  |
| Y          |  | 1-18                  |

Further documents are listed in the continuation of box C.

Patent family members are listed in annex.

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Date of the actual completion of the international search

Date of mailing of the international search report

30 July 1999

17/08/1999

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2  
 NL - 2280 HV Rijswijk  
 Tel. (+31-70) 340-2040, Tx. 31 651 epo nl.  
 Fax: (+31-70) 340-3016

Authorized officer

Stoltner, A

## INTERNATIONAL SEARCH REPORT

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## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

| Category | Citation of document, with indication, where appropriate, of the relevant passages   | Relevant to claim No. |
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| A        | WO 96 38153 A (SEARLE & CO ;KARARLI TUGRUL T (US); OTTO DAVID (US); PENZOTTI STAN)<br>5 December 1996 (1996-12-05)<br>*cf. abstract and page 3, "summary of the invention", lines 1-26, page 4, lines 12-34 and page 5, first line*<br>-----   | 1-18                  |
| A        | G. BUCKTON ET AL.: "The use of isothermal microcalorimetry in the study of changes in crystallinity of spray-dried salbutamol sulfate"<br>INTERNATIONAL JOURNAL OF PHARMACEUTICS,<br>vol. 116, no. 1,<br>14 March 1995 (1995-03-14), pages 113-118,<br>XP002110839<br>*cf. abstract, page 116, left col., 2nd para. and right col., lines 1-12*<br>----- | 1-18                  |

# INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

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| Patent document cited in search report |   | Publication date | Patent family member(s)   | Publication date   |
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| WO 9638153                             | A | 05-12-1996       | AU 5794196 A<br>CA 2222811 A<br>EP 0828495 A  | 18-12-1996<br>05-12-1996<br>18-03-1998   |